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A scoping review of worldwide guidelines for diagnosis and treatment of Helicobacter pylori infection

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Abstract

Background This study comprehensively analyzes the diagnostic criteria, eradication indications, treatment, and other information in the latest guidelines published by various countries around the world, so that researchers can have a systematic understanding of Helicobacter pylori and further provide a basis for clinical H. pylori diagnosis and treatment.

Methods Nine online databases were searched to find the latest version of guidelines for H. pylori worldwide. Two researchers read the included guidelines independently and extracted the eradication indications, diagnostic criteria, and treatment in the guidelines, conducting a summary of them.

Results A total of 25 guidelines or consensus were included. Among all diagnostic methods for H. pylori infection, the urea breath test is widely recommended as the first choice. A total of 20 guidelines mentioned indications for H. pylori eradication. Among them, the indications with a higher proportion of recommendations were long-term use of non-steroidal anti-inflammatory drugs (including low-dose aspirin) in 90% of patients with peptic ulcer history or active peptic ulcer disease 80%; gastric mucosa-associated lymphoid tissue (MALT) lymphoma 75%. It is worth mentioning that 40% of the guidelines pointed out that, as long as H. pylori infection is confirmed, it should be eradicated. A total of 24 guidelines mentioned treatment for H. pylori. Among them, bismuth quadruple therapy (a combination of a bismuth, two antibiotics, and a proton pump inhibitor (PPI)) was the most recommended first-line therapy. Levofloxacin triple therapy (a combining of a bismuth, an antibiotic, and a PPI) was the most recommended second-line therapy.

Conclusion Current global Helicobacter pylori management guidelines share foundational consensus, yet exhibit regional variations in diagnostic criteria, eradication indications, and therapeutic regimens due to context-specific epidemiological, socioeconomic, and antimicrobial resistance profiles. Clinical practice should prioritize regionally tailored approaches, integrating local guidelines while maintaining awareness of international recommendations to optimize decision-making. Moreover, health authorities responsible for guideline development must ensure timely updates based on dynamic surveillance of local resistance patterns and socioeconomic realities.

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Background

Helicobacter pylori is a gram-negative bacterium that is microaerophilic. It has a strong viability and can adapt to an acidic environment. It is mainly distributed in the gastric mucosa and is the only bacterium found to survive in the stomach so far [1]. H. pylori infection may last a lifetime, and there is a possibility of recurrence after eradication treatment [2]. A study has shown that in the 10 years from 2011 to 2021, the recurrence rate of H. pylori infection in the world was 9% (95% CI, 8–11%) [3]. In addition, a variety of gastric diseases such as atrophic gastritis and peptic ulcer have been shown to be related to H. pylori in previous studies [4]. Eradication of H. pylori can reduce the occurrence and development of gastric cancer and MALT lymphoma, which are high in morbidity and mortality [4].

The global prevalence of H. pylori infection remains high, with a 2018 meta-analysis reporting an overall rate of 44.3% [5]. Another 2017 meta-analysis reported regional disparities ranging from 70.1% in Africa to 24.4% in Oceania [6]. Country-specific variations are also evident, such as Indonesia's infection rate of 10.10% in 2020, which was reported by another epidemiological study [7].

Antibiotic resistance, a leading cause of H. pylori treatment failure [8, 9], exhibits marked geographical heterogeneity. A global systematic review ($n=178$ studies) among 65 countries revealed low resistance rates to amoxicillin and tetracycline, contrasted with high metronidazole resistance. Notably, clarithromycin resistance in India remains low despite elevated amoxicillin resistance [10]. Both the global prevalence of H. pylori infection and the patterns of antibiotic resistance are comprehensively illustrated in Fig. 1.

Geographical heterogeneity in H. pylori management guidelines, shaped by differences in population demographics, socioeconomic factors, and antimicrobial resistance profiles, is widely recognized but remains underexplored. While existing systematic reviews are limited by outdated evidence bases (with literature searches by 2021 [11]) and narrow scopes (e.g., analyzing only 17 [11] or 13 [12] guidelines), our study addresses these limitations by synthesizing a broader range of updated guidelines (2014–2024). This comprehensive comparison across multiple dimensions, including diagnostic criteria, treatment strategies, and eradication indications, provides clinicians with a consolidated resource for accessing key differences in guidelines worldwide.

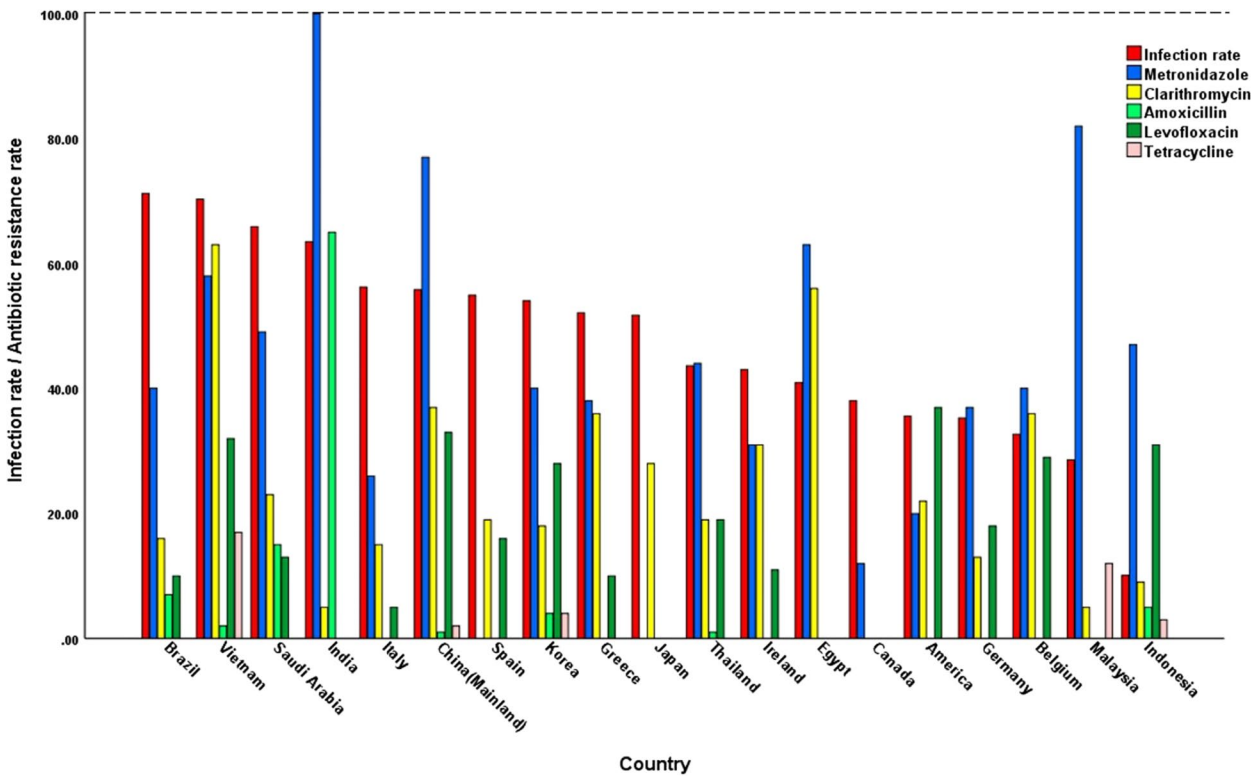

Fig. 1 Statistics of Helicobacter pylori infection rate and drug resistance in different countries. *Data in Figure 1 are sourced from: A 2017 meta-analysis [6] for infection rates (excluding Indonesia); A 2020 study [7] for Indonesia's infection rate; A global systematic review [8] for antibiotic resistance data

Furthermore, our findings offer actionable insights for health authorities to refine local guidelines and inform the development of contextually tailored strategies, bridging the gap between global evidence and region-specific implementation challenges.

Methods

Development of the systematic search strategy

Six online databases were retrieved, including CNKI, PubMed, Web of Science, Wiley Online Library, Wanfang database, and China Science and Technology Journal Database. At the same time, we also consulted the three professional guideline websites of GIN (Guidelines International Network), NICE (National Institute for Health and Clinical Excellence), and SIGN (Scottish Intercollegiate Guidelines Network).

The search strategy was developed and executed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, as detailed in Supplementary Table S2.

The following terms were searched in the title of the articles: Helicobacter pylori, H. pylori, Helicobacter, guideline, guidance, recommendation, statement, and consensus. The guidelines were dated between 2014.1.1 and 2025.2.19.

Inclusion and exclusion criteria for guidelines:

1) The guidelines or consensus included in our article were published in Chinese or English.
2) For countries, regions, or organizations that identified multiple guidelines, we selected the most recent versions.
3) If the treatment plans given by different institutions in the same country were completely consistent, the most widely used version was retained.
4) Exclude guidelines for children or teenagers only.

During the search procedure, no specific selection of guidelines from particular countries or regions was made. All relevant guidelines identified through database searches and meeting inclusion criteria were included in the analysis. The detailed flowchart of the search process is presented in Fig. 2.

Standardization of data extraction procedures

Two researchers independently reviewed the guidelines included in this study to extract indications, diagnostic criteria, and treatment recommendations (including first-line, second-line, and rescue therapies) for H. pylori. The two researchers reviewed their findings together and reached consensus on all extracted data.

Assessment of clinical guideline quality

The methodological quality assessment of Helicobacter pylori management guidelines was conducted using the validated Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument [13]. Two independent evaluators (Sun M.Y., Liu E.Y.) performed critical appraisals in strict accordance with the AGREE II operational manual. Scoring discrepancies were resolved through a standardized protocol: when inter-rater variances occurred, a structured deliberation with a senior researcher (Han M.) was applied. To ensure impartiality, Han M. had no prior involvement in guideline assessments and independently verified all contested items against AGREE II criteria before final determination.

Each guideline domain was systematically rated on a 7-point Likert-type scale (1 = strongly disagree; 7 = strongly agree), with point allocation predicated on the comprehensiveness and methodological rigor of guideline reporting. Final domain scores were calculated using the standardized formula: (Obtained score − Minimum possible score)/(Maximum possible score − Minimum possible score) × 100%. Higher percentage scores reflect superior compliance with established methodological standards.

Application of statistical analysis tools

This study used SPSS 22.0 software to calculate the intraclass correlation coefficient (ICC) to determine the rating heterogeneity between the two raters [12]. If the ICC > 0.75, it means that the consistency of the study is high; if the ICC is between 0.60 and 0.74, it means that the consistency of the study is high; if the ICC is between 0.40 and 0.59, it means that the consistency of the study is average; if the value is < 0.40, This shows that the research consistency is poor.

Results

Characteristics of included clinical guidelines

A total of 590 publications were initially retrieved. After deduplication and screening, 26 articles comprising the latest global guidelines or consensus published by authoritative organizations from 2014 to 2024 were included [14–39]. Among these 26 articles, two guidelines were international in scope, while two articles constituted distinct sections of the same Chinese guideline (treatment and non-treatment components) that were analyzed collectively as a unified entity. Consequently, the final synthesis encompassed 25 discrete clinical guidelines. The entire literature selection and consolidation process is schematically illustrated in Fig. 2. These documents systematically addressed

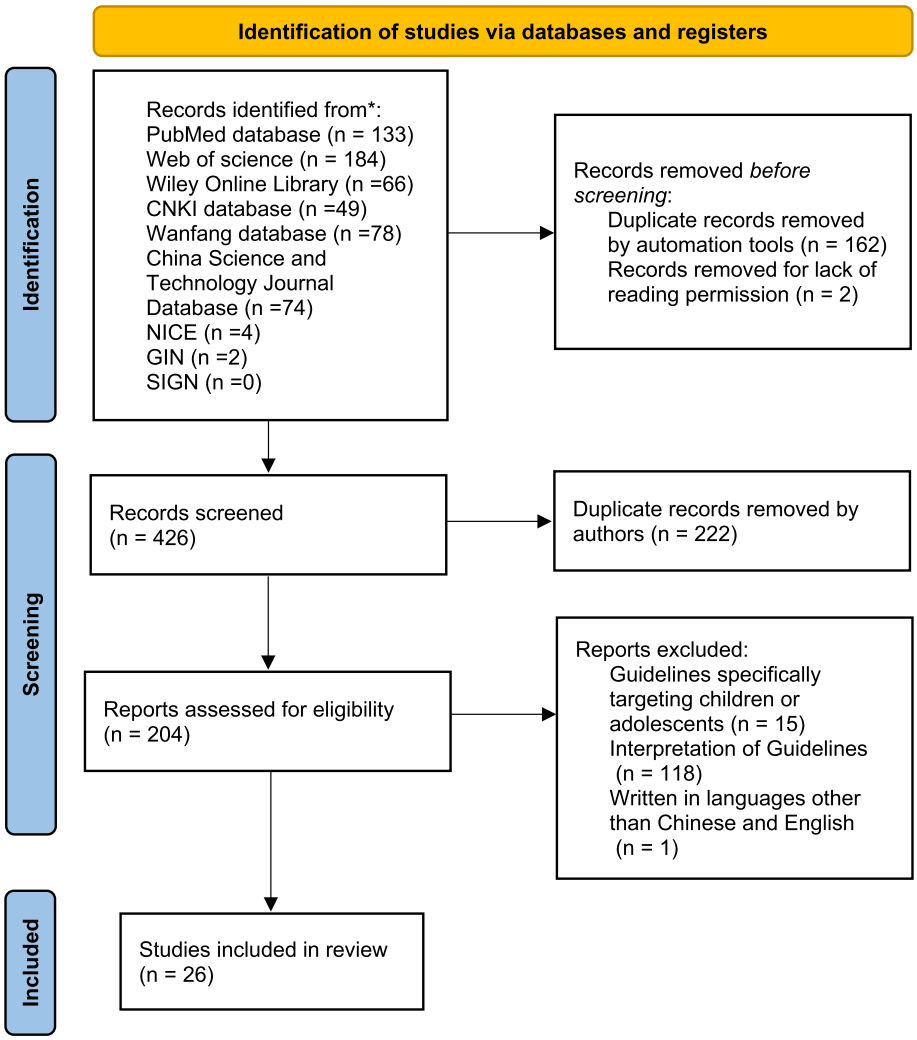

Fig. 2 PRISMA 2020 flow diagram

evidence-based recommendations for H. pylori infection, with a focus on indications, diagnostic criteria, and therapeutic strategies.

Evaluation of guideline quality ratings

The median scores for the domain of "scope and purpose" and "clarity of presentation" were high, respectively at 91.67% (range from 72.22 to 100.00%) and 94.44% (range from 66.67 to 97.22%). The result shows that most existing guidelines are clear about the purpose of formulating the guideline, and can well put forward the clinical problems and the target population for it. At the same time, the suggestions given by most guidelines are clear and easy to identify. The median scores for the domain of "editorial independence" were also high, at 91.67% (range from 29.17 to 100.00%).

The median scores of the other three domains were relatively low. For "stakeholder involvement", "rigor of development" and "applicability", the median scores were respectively at 61.11% (range from 44.44 to 100.00%), 66.67% (range from 26.04 to 89.58%), and 58.33% (range from 37.50 to 81.25%). The reason for the generally low score in the "stakeholder involvement" part is that most of the guidelines do not explicitly mention the inclusion of methodological experts in the development process, with only the 2021 Spanish guideline and the 2020 Korea guideline mentioning this. For the part of "rigor of development", 2015 Thailand's guideline and 2022 Saudi Arabia's guideline scored low because the evidence search strategy and methodology for recommendations were not described in the guidelines, and these guidelines were not reviewed by external experts before they were published (at least not in the text). The score in applicability was low for all guidelines because they did not provide advice and/

Table 1 Quality scores of guidelines

Country/category	Scope and purpose	Stakeholder involvement	Rigor of development	Clarity of presentation	Applicability	Editorial independence	ICC
Latin America 2014 [14]	88.89%	55.56%	73.96%	80.56%	58.33%	41.67%	0.902
Thailand 2015 [15]	75.00%	44.44%	45.83%	66.67%	37.50%	41.67%	0.930
Canada 2016 [16]	94.44%	69.44%	86.46%	94.44%	54.17%	100.00%	0.929
Japan 2016 [17]	94.44%	50.00%	85.42%	94.44%	56.25%	100.00%	0.903
America 2018 [18]	97.22%	97.22%	66.67%	88.89%	56.25%	100.00%	0.933
Brazil 2018 [19]	91.67%	63.89%	60.42%	94.44%	66.67%	91.67%	0.901
Egypt 2018 [20]	91.67%	47.22%	56.25%	94.44%	50.00%	45.83%	0.910
ASEAN 2018 [21]	86.11%	47.22%	63.54%	91.67%	54.17%	62.50%	0.923
Korea 2020 [22]	97.22%	91.67%	89.58%	94.44%	60.42%	95.83%	0.93
Spanish 2021 [23]	88.89%	75.00%	69.79%	94.44%	58.33%	100.00%	0.915
India 2021 [24]	72.22%	44.44%	59.38%	88.89%	62.50%	100.00%	0.932
Greece 2021 [25]	80.56%	61.11%	64.58%	86.11%	58.33%	58.33%	0.927
Italy 2022 [26]	91.67%	61.11%	80.21%	91.67%	64.58%	29.17%	0.900
Saudi Arabia 2022 [27]	83.33%	44.44%	26.04%	94.44%	54.17%	91.67%	0.911
Maastricht VI 2022 [28]	88.89%	50.00%	53.13%	97.22%	64.58%	95.83%	0.941
Vietnam 2022 [29]	88.89%	44.44%	65.63%	91.67%	58.33%	100.00%	0.930
China 2022 [30, 31]	77.78%	61.11%	75.00%	97.22%	64.58%	95.83%	0.924
Indonesia 2022 [32]	94.44%	77.78%	83.33%	94.44%	79.17%	95.83%	0.920
WGO 2023 [33]	91.67%	55.56%	42.71%	91.67%	66.67%	91.67%	0.918
Belgium 2023 [34]	72.22%	55.56%	76.04%	94.44%	62.50%	41.67%	0.927
Malaysia 2023 [35]	97.22%	61.11%	63.54%	94.44%	58.33%	83.33%	0.907
Africa 2024 [36]	86.11%	52.78%	60.42%	91.67%	64.58%	100.00%	0.951
Germany 2024 [37]	100.00%	100.00%	71.88%	94.44%	43.75%	100.00%	0.948
Ireland 2024 [38]	91.67%	69.44%	67.71%	97.22%	58.33%	87.50%	0.927
ACG 2024 [39]	100.00%	86.11%	85.42%	100.00%	81.25%	91.67%	0.927

or tools on how the recommendations can be put into practice. The exact quality scores are shown in Table 1.

The score heterogeneity evaluations (ICC) of the two researchers were both higher than 0.9, indicating a high degree of consistency in the evaluation results.

Distribution of evidence grading methodologies

A total of 17 guidelines or consensus [15–18, 21–23, 28–31, 34, 35, 37–39] were based on the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system to measure the level of evidence and strength of recommendation. Among the remaining guidelines and consensus, 1 article adopted the evaluation method of the US Preventive Services Task Force [14]; 1 article adopted the standards stipulated by the Brazilian Medical Guidelines Association [19]; 1 article adopted the Canadian Regular Health Examination Standard Working Group Evaluation [24]; 5 articles did not have clear evaluation criteria in the guidelines or consensus.

Comparison of eradication indications

A total of 21 guidelines or consensus mentioned the indications for H. pylori eradication. The 2015 Kyoto Consensus [40] first proposed that as long as individuals with H. pylori infection are detected, H. pylori should be eradicated. Among the 21 guidelines, the indications recommended by more than half of the guidelines include: long-term use of non-steroidal anti-inflammatory drugs (including low-dose aspirin), gastric MALT lymphoma, past or current patients with gastric ulcer or duodenal ulcer, unexplained iron deficiency anemia, idiopathic thrombocytopenic purpura, early gastric cancer after resection, uninvestigated dyspepsia, high risk of gastric cancer. The specific recommended indications for H. pylori eradication and recommended rate are shown in Table 2.

Notably, gastroesophageal reflux disease (GERD) demonstrated divergent recommendations across guidelines: The 2016 Japanese guideline [17], the 2018 ASEAN consensus [21], 2022 Italian [26], 2022 Vietnamese guideline [29], 2022 Indonesian guideline [32], and 2023 WGO

Table 2 Summary of eradication indications

Indications/area (year)	Thailand 2015 [15]	Japan 2016 [18]	ASEAN 2018 [21]	America 2016 [17]	Brazil 2018 [19]	Egypt 2018 [20]	Korea 2020 [22]	Greece 2021 [25]	India 2021 [24]	China 2022 [30, 31]	Maastricht VI 2022 [28]
Long-term use of NSAIDs (including low-dose aspirin) and have a prior history of gastro-duodenal ulcers or bleeds	R		R	R	R	R	R	R	R	R	R
Peptic ulcer disease (prior history or active disease)	R	R		R		R	R	R	R	R	
Gastric MALT Lymphoma	R	R	R	R		R			R	R	R
Unexplained iron deficiency anemia		R			R		R	R	R	R	R
Idiopathic thrombocytopenic purpura		R		R	R		R	R	R		R
Early gastric tumors have been treated	R	R	R[b]				R	R	R	R	
Uninvestigated dyspepsia	R[c]		R	R	R[a]	R		R			R
People at high risk of stomach cancer	R		R	R		R		R		R	
Long-term use of PPIs				R				R	R	R	R
Idiopathic vitamin B12 deficiency					R		R	R	R	R	R
Helicobacter pylori infection was confirmed				R		R				R	
Gastroesophageal reflux disease	NR	R	R	R					NR		
Functional dyspepsia		R					R	R			

Table 2 (continued)

Indications/area (year)	Saudi 2022 [27]	Italy 2022 [26]	Vietnam 2022 [29]	Indonesia 2022 [32]	Belgian 2023 [34]	Malaysia 2023 [35]	WGO 2023 [33]	Africa 2024 [36]	Germany 2024 [37]	ACG 2024 [39]	Recommended rate ($n = 21$)
Long-term use of NSAIDs (including low-dose aspirin) and have a prior history of gastro-duodenal ulcers or bleeds	R	R	R	R	R		R	R	R	R	19/21
Peptic ulcer disease (prior history or active disease)	R		R	R	R	R	R	R	R	R	17/21
Gastric MALT lymphoma	R		R	R	R	R	R		R	R	16/21
Unexplained iron deficiency anemia	R	R	R	R	R		R		R	R	15/21
Idiopathic thrombocytopenic purpura	R		R	R	R		R		R	R	14/21
Early gastric tumors have been treated	R		R		R		R		R		12/21
Uninvestigated dyspepsia		R	R		R[a]	R			R[a]	R	13/21
People at high risk of stomach cancer	R		R			R	R		R	R	12/21
Long-term use of PPIs				R	R		R	R	R		10/21
Idiopathic vitamin B12 deficiency	R	R									8/21
Helicobacter pylori infection was confirmed	R						R[d]	R	R	R	8/21
Gastroesophageal reflux disease	R	R	R	R			R		NR		8/21

Table 2 (continued)

Functional dyspepsia	R	R	R	R	7/21

NR not recommend, *R* recommended

[a] The original paper only mentioned dyspepsia

[b] Including all gastric precancerous lesions

[c] Indigestion where antisecretory drugs are ineffective

[d] Helicobacter pylori eradication is determined according to the patient's wishes

guideline [33] endorsed eradication specifically for GERD patients requiring prolonged proton pump inhibitor therapy. Conversely, the 2015 Thai guideline [15], 2024 German update [37], and 2021 Indian guideline [24] explicitly advised against routine eradication in GERD management.

Some indications were recommended by only one or two guidelines. To ensure the clarity and conciseness of data presentation, these indications were not included in the table. They consist of the following: gastric erosions [15]; Alzheimer's disease [17]; chronic urticaria [17]; Parkinson's syndrome [17]; cap polyposis [17]; diabetes mellitus [17]; rectal MALT lymphoma [17]; Diffuse Large B-cell lymphoma (DLBCL) [17]; lymphocytic gastritis [37]; Menetrier's disease [37]; first-generation individuals from areas with high prevalence of H. pylori [18]; people with a family history of peptic ulcer disease [18]; marginal zone B-cell lymphoma [22]; atrophy of gastric mucosa or intestinal metaplasia [22]; patients prior to bariatric surgery (refers to gastric bypass surgery for weight loss) [34].

Comparison of diagnosis and eradication detection criteria

A total of 23 guidelines or consensus involved diagnostic methods for H. pylori, and the remaining 3 guidelines did not [16, 22, 26]. The urea breath test is recommended by 23 guidelines as the first choice for diagnosis. The stool antigen test was in second place as it was recommended unanimously by 23 guidelines or consensus. Other recommended alternatives include: serology, rapid urease test, and cell biology test.

Notably, 7 guidelines (Thailand 2015; America 2018; India 2021; Italy 2022; Vietnam 2022; WGO 2023; Germany 2024) [15, 18, 24, 26, 29, 33, 37], explicitly contraindicated serological testing due to its inability to differentiate active versus past infections. This contrasts sharply with 11 guidelines (ASEAN 2018; Brazil 2018; Egypt 2018; Greece 2020; Indonesia 2022; Saudi Arabia 2022; Maastricht VI 2022; Belgium 2023; Malaysia 2023; Africa 2022; Ireland 2024) [19–21, 25, 27, 28, 32, 34–36, 38] that conditionally recommended serology based on cost-effectiveness considerations, though with varying restrictions. For instance, the Maastricht VI guideline strictly limited serological application to post-endoscopy supplementary testing.

For eradication, a total of 21 guidelines involved methods for detecting successful H. pylori eradication, while the remaining five guidelines [16, 22, 26, 34, 36] did not. In the guidelines that clearly stated the eradication detection method, the urea breath test was consistently recommended as the first priority, and the stool antigen test was recommended as the second choice. The rapid urease test is unanimously not recommended as a method for detecting successful H. pylori eradication.

Comparison of treatment strategies

The treatment plan is divided into first-line treatment and other forms of treatment. Other treatment options include second-line treatment, third-line treatment, and rescue therapy. Table 3 in the main text exclude the regimens only recommended by one guideline. Detailed treatment information is given in Supplementary Table S1, including drug dosage, duration, and frequency of medication.

It is worth noting that the newly released 2024 ACG guideline [39] recommends the use of potassium-competitive acid blockers (PCABs) in dual or triple therapy regimens as first-line treatment options.

The first-line treatment mostly accepted worldwide is the standard bismuth quadruple therapy (recommendation rate 18/24), and the drug composition is proton pump inhibitor (PPI), bismuth, metronidazole, and tetracycline. In the second place, traditional triple therapy is recommended. The drug composition is PPI, amoxicillin, and clarithromycin. The recommendation rate of traditional triple therapy was 17/24, of which 13/24 guidelines or consensus only used this method in areas known to have low clarithromycin resistance. In addition, concomitant therapy consisting of four drugs (PPI, amoxicillin, metronidazole, and clarithromycin) was recommended by half of the guidelines (12/24).

The recommended rate of levofloxacin triple therapy is 16/23 and it is the highest in the second-line treatment. The recommended rate of bismuth-containing quadruple therapy was 14/23 when the first-line treatment did not use this therapy for eradication. The recommended rate of rifabutin triple therapy (PPI, amoxicillin, rifabutin) was 11/23.

Among all the above-mentioned treatments, there are 209 treatment plans with a clear course of treatment ranging from 7 to 14 days. Among them, the most recommended course of treatment is 14 days. However, the most recommended course of treatment in sequential therapy is 10 days.

In the guidelines providing information regarding drug doses, the doses of 6 PPIs involved are: omeprazole 20 mg, pantoprazole 40 mg, esomeprazole 20 or 40 mg, lansoprazole 30 mg, rabeprazole 20 mg or 40 mg, Vonorazan 20 mg. The medication is taken twice a day. The bismuth agents involved mainly include bismuth subsalicylate, bismuth subcitrate, colloidal bismuth pectin, etc. The doses range from 120 to 300 mg, and the medication is taken two to four times a day.

The doses of antibiotics used in each guideline vary. The dosage range of amoxicillin is 2000–4500 mg each day, and the dosage recommended by most guidelines is 1000 mg each time, twice a day. The dosage range of clarithromycin is 500–1000 mg each day, and most

Table 3 Summary of treatments

Therapy	First-line recommendation ($n=24$)		Second-line recommendation ($n=23$)	
Triple therapy				
P + A + C (Low resistance of C)	Canada, Indonesia, ACG, ASEAN, Egypt, Korea, India, Maastricht VI, Italy, WGO, Belgium, Africa, Ireland	13/24	Brazil, Germany, Ireland	3/23
P + A + C	Latin America, Japan, Brazil, Malaysia	4/24		
P + C + M (Low resistance of C)	Thailand[a], Canada, WGO[a]	3/24	/	/
P + C + M	Latin America, Japan[a], India[a], Malaysia[a]	5/24		
P + A + M	Canada, Japan, ASEAN, Korea	4/24	India	1/23
P + A + L (Low resistance of L)	Latin America, ASEAN	3/24	Latin America, Thailand, Canada, ACG, Brazil, Egypt, Korea, Greece, India, Maastricht VI, Italy, Malaysia, WGO, Africa, Germany	16/23
P + A + R	ACG	/	Canada, ACG, ASEAN, Korea, Greece, India, Maastricht VI, Italy, WGO, Belgium, Ireland, Indonesia	11/23
P + A + Ti	Canada, ASEAN	2/24	/	/
P + C + L	Brazil[a], Greece[a]	2/24	India[a]	1/23
P + A + S	/	/	Japan, Korea	2/23
P + A + Mo	/	/	Korea, Greece, India	3/23
Bismuth-based quadruple therapy				
P + B + M + T	Thailand[a], Canada[a], Indonesia[a], Ireland, ACG[a], ASEAN[a], Brazil[a], Korea[a], Spanish[a], India[a], Maastricht VI[a], China[a], Saudi[a], Vietnam, Malaysia, WGO[a], Belgium[a], Germany	18/24	Thailand, Canada, Ireland, ACG, Brazil, Egypt, Korea, Spanish[a], India, Greece[a], Saudi, Vietnam, WGO, Africa	14/23
P + B + A + M	ASEAN, China	2/24	/	/
P + B + A + T	India, China	2/24	/	/
P + B + A + L	China, Vietnam	2/24	ASEAN, Brazil, Korea, Spanish, India, Maastricht VI, Vietnam, Africa, Ireland	9/23
P + B + C + L	China[a]	1/24	Spanish[a]	1/23
Concomitant quadruple therapy				
P + A + C + M	Latin America, Thailand, Canada, ASEAN, Brazil, Korea, Spanish, Greece, Maastricht VI, Saudi, WGO, Belgium, Indonesia	12/24	Latin America, Korea, Spanish	3/23
P + A + C + Ni	Saudi	2/24	Egypt	2/23
P + A + C + Ti	Latin America, ASEAN, Brazil, Saudi, Italy	5/24	Latin America, Italy	2/23
Sequential therapy				
P + A/P + C + M	Latin America, Thailand, Korea, India	4/24	/	/
P + A/P + A + C + M	ASEAN, Greece, Africa	3/24	/	/
P + A/P + C + Ti	Latin America, Italy	2/24	Italy	1/23
High-dose therapy				
P + A	China, Malaysia	2/24	Japan, ACG 2017, ASEAN, Korea, Maastricht VI, Italy, Malaysia, WGO, Indonesia	8/23

[a] Patients with penicillin allergy can also use this therapy

A represents amoxicillin, *B* represents bismuth, *C* represents clarithromycin, *L* represents levofloxacin, *M* represents metronidazole, *Mo* represents moxifloxacin, *P* represents PPI, R represents rifabutin, *S* represents sitafloxacin, *T* represents tetracycline, and *Ti* represents tinidazole

guidelines recommend a dosage of 500 mg each time, twice a day. The dosage range of metronidazole is 375–2000 mg each day, and the dosage recommended by most guidelines is 500 mg each time, twice a day in triple therapy, concomitant therapy, and sequential therapy. For quadruple therapy that involves metronidazole, the recommended dose is 400–500 mg each time, 3 to 4 times a day. The dosage range of tetracycline is 500–2000 mg each day, and the dosage recommended by most guidelines is 500 mg each time, 3 to 4 times a day. The dosage range of levofloxacin is 250–1000 mg each day, and most guidelines recommend a dosage of 500 mg each time, once a day.

Discussion

Variations of H. pylori infection rates

The infection rate of Helicobacter pylori in the world is relatively high, with notable variations across regions.

In Asia, excluding Indonesia, the infection rate is generally higher compared to Europe. These differences can be attributed to various factors, including geographical environments, economic and medical conditions, ethnic compositions, socioeconomic statuses, lifestyle habits, and other regional disparities. Developing countries exhibit a significantly higher overall infection rate of 50.8% compared to developed countries at 34.7% [6], underscoring the impact of social environments on infection rates.

In contrast, Indonesia stands out as an exception within developing countries due to its notably lower infection rate. Several factors contribute to this phenomenon. Genetic differences between ethnic groups and variations in regional H. pylori strain types play significant roles. Additionally, local environmental factors, such as diet, lifestyle habits, and cultural practices, are critical contributors to the reduced infection rates. The predominant Javanese and Sundanese populations in Indonesia exhibit unique cultural practices that influence H. pylori transmission dynamics [41]. One key dietary practice in Indonesia is the consumption of "Centella asiatica," which has been shown to potentially protect the gastric mucosa [42] and exhibit anti-H. pylori effects [43]. The combined factors of genetic, environmental, dietary, and microbial influences are believed to collectively contribute to the generally lower infection rates observed in Indonesia compared to other developing countries.

Variations of eradication indications

The indications for H. pylori eradication in most guidelines are relatively consistent, but it is controversial whether gastric reflux esophagitis should be included in the indications for eradication.

Japan's 2016 guideline [17], ASEAN's 2018 guideline [21], Italy's 2022 guideline [26], Vietnam's 2022 guideline [29], and WGO's 2023 guideline [33] considered gastroesophageal reflux disease as an indication for eradication when patients need long-term PPI therapy. Precisely, the 2016 Japanese guideline [17] believes that long-term use of PPIs will worsen the symptoms of gastritis and gastric mucosal atrophy, leading to an increased risk of gastric cancer. Saudi Arabia's 2022 guideline [27] believes that gastroesophageal reflux disease can be used as one of the indications for eradication, but it is still controversial. America's 2018 guideline [18] considered that H. pylori testing should only be performed in patients with gastroesophageal reflux disease if they are at high risk of H. pylori-related diseases.

However, Thailand's 2015 guideline [15], Germany's 2024 guideline [37], Indonesia's 2021 guideline [32], and India's 2021 guideline [24] concluded that eradication of Helicobacter pylori is not recommended for patients with gastroesophageal reflux disease. The 2021 guideline in India [24] believes that the prevalence of H. pylori is inversely related to the occurrence of gastric reflux esophagitis and related diseases, which suggests that H. pylori has a protective effect on gastric reflux esophagitis. Another study showed an increased prevalence of reflux esophagitis after successful H. pylori eradication was compared with patients with persistent H. pylori infection. However, there was no significant difference in reflux symptoms between those with persistent infection and those without H. pylori infection [44].

Variations of diagnostic methodologies

Serological testing is controversial as a diagnostic method of H. pylori. The guidelines that do not recommend serological testing believe that serological antibody testing cannot determine whether H. pylori is an active infection or a past infection. For example, the 2018 America Consensus [18] pointed out that antibodies produced in the body after H. pylori eradication can keep serological tests positive for decades. However, most guidelines recommending serological testing are based on cost-effectiveness considerations. For example, the 2018 Brazilian guideline [19] pointed out that locally validated serological testing is the preferred method for population-based primary screening studies. Special consideration should be given in clinical situations. Examples include gastrointestinal bleeding, atrophic gastritis, gastric mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer, where initial screening does not yield false negative results. Serological tests have the advantages of being non-invasive, widely available, inexpensive, easy to perform, and widely accepted by patients. In 2022, the Maastricht VI guideline [28] pointed out that serological testing is more suitable as a supplementary testing method after microscopic examination.

Variations of treatment strategies

With increasing antibiotic resistance, bismuth quadruple therapy and concomitant therapy are replacing classical triple therapy as a first-line treatment. The current data show that, although the recommendation rate of classical triple therapy is the highest, the guidelines recommending this therapy are mostly used in areas where the clarithromycin resistance is known to be less than 15%, so the universality of classical triple therapy is decreasing.

In the triple therapy of first-line treatment, the recommendation rate of amoxicillin and metronidazole triple combination is significantly higher in Asia than in Europe. The reason may be economic. The proportion of

developing countries in Asia is relatively large, and metronidazole is more cost-effective for clinical application after comprehensive consideration of the cost and efficacy. From a drug resistance perspective, Asian countries have generally high resistance to metronidazole, with some of the countries having 100% metronidazole resistance. In India's 2012 guideline, the reasons for the high drug resistance of metronidazole in Asia (mainly China and India) include: low economic cost; easy access as an over-the-counter drug; widely used in antidiarrheal agents and treatment of functional bowel disease [45]. It is worth noting that the 2024 ACG guideline [39] recognizes that clinicians may not have access to clarithromycin susceptibility testing, particularly when treating treatment-naive patients. In such cases, the decision to include clarithromycin in a treatment regimen is essentially empiric. If clarithromycin susceptibility is unknown and the patient has no history of macrolide use, clarithromycin-containing triple therapy may be considered if no alternative first-line therapy is available. This regimen includes clarithromycin, amoxicillin, and a PCAB rather than a PPI.

Limitations of this study

First, the countries or organizations included in this review are not comprehensive. We retrieved and included guidelines from 20 countries, as well as drug resistance and epidemiological data from these areas. This does not fully represent the current status of H. pylori infection worldwide. Follow-up studies can further explore the epidemiological information of H. pylori in the countries or regions and the current status of guidance documents that are not included in our article.

In some large countries, differences between regions within the country may be ignored. In this review, all guidelines are based on countries or organizations, and sub-regions under these units are not considered. For example, China's southeast coastal cities and northwest inland cities have large differences in climate, geography, economic and medical level, etc. Strictly speaking, we cannot use the average level of a country to represent these different sub-regions. So, it should be noted that the conclusions of this study should be limited to only the level between countries.

Although we have selected the latest guidelines of each country, there are still large differences in the time span of the guidelines. Among the latest guidelines we have selected, some guidelines have been recently updated (such as the 2024 ACG guideline [39]), while some guidelines are still relatively old (such as the 2014 Latin American guideline [14]), which may make the guidelines' horizontal comparison between them lack certain accuracy.

Given the variations in guideline publication timing and regional resistance patterns, clinical practice should adapt H. pylori management strategies based on local resistance data while also considering socioeconomic factors in different settings.

Additionally, the infection rate data for Indonesia was sourced from a 2020 epidemiological study, whereas data for other countries were derived from a 2017 meta-analysis. The temporal discrepancy in these datasets may introduce potential biases when making cross-country comparisons; To ensure data completeness, the dataset from this article can be referenced for further validation and analysis.

In terms of the methodology of the guidelines and consensus, the evidence evaluation and recommendation levels in 4 guidelines or consensus were not evaluated using the GRADE system. 5 guidelines or consensus did not mention the formulation method. Inconsistent methodological standards may lead to slight differences in the evaluation systems between different guidelines, but the obtained data still maintain a certain reference value and clinical significance among countries.

Limitation of methodological quality of the H. pylori guidelines

The findings of the current study revealed notable variability and deficiencies across three critical domains of guideline quality: stakeholder involvement, the rigor of development, and applicability. These results highlight systemic challenges in current guideline development practices. The suboptimal median score for stakeholder involvement (61.11%) underscores a widespread failure to integrate methodological experts into guideline panels, as evidenced by the limited adherence to this criterion in most guidelines except those from Spain (2021) and Korea (2020). (However, it is possible that some guidelines involved methodological experts during their development but did not explicitly document this in their methodology sections, which may partially account for the observed scores.) This omission may compromise the methodological credibility and contextual relevance of recommendations. And the absence of explicit stakeholder engagement strategies could further diminish guideline acceptance among end-users.

Similarly, the modest performance in the rigor of development, with a median score of 66.67%, particularly in guidelines from Indonesia (2017), Thailand (2015), and Saudi Arabia (2022), reflects inadequate transparency in evidence synthesis and recommendation formulation. The lack of documented search strategies or external review processes raises concerns about potential biases and undermines the reproducibility of these guidelines. Such shortcomings contradict established standards for

trustworthy guidelines, which mandate rigorous methodology and external validation to ensure objectivity [46]. The low scores in these cases suggest that resource constraints or insufficient institutional oversight may hinder adherence to internationally recognized development protocols, particularly in resource-limited settings.

The uniformly poor performance in applicability (median 58.33%) further exposes a critical gap between guideline creation and real-world implementation. The absence of practical tools or contextualized advice renders recommendations theoretically sound but operationally inert. Without actionable strategies to address barriers (e.g., training modules, monitoring frameworks, or cost-effectiveness analyses), guidelines risk remaining underutilized, regardless of their clinical validity.

Collectively, these findings align with global critiques of guideline quality but also highlight region-specific challenges, particularly in integrating methodological rigor and stakeholder diversity. Future efforts should prioritize structured frameworks for multidisciplinary collaboration, standardized reporting of evidence-to-decision processes, and the integration of implementation science principles during guideline development. Additionally, fostering international partnerships to share best practices, particularly for external review and applicability planning, could help mitigate disparities in guideline quality across regions.

Future prospects

The findings of this study, while informative, reveal critical opportunities for advancing research in this field. First, expanding the geographic scope beyond the current dataset could enhance the generalizability of insights, particularly by incorporating underrepresented regions. Second, future studies should prioritize granular analyses of intra-national disparities, such as socioeconomic or infrastructural differences between coastal and inland regions in large nations like China, to better capture localized challenges. Additionally, addressing temporal inconsistencies in guideline updates, where some regions adopt cutting-edge revisions while others rely on outdated frameworks, will be vital for ensuring equitable global health practices. Finally, establishing harmonized methodological standards across guideline development processes could mitigate variability in quality and implementation. These directions underscore the importance of fostering international collaboration to address regional inequities and systematize evidence-based approaches in H. pylori management.

Addressing Helicobacter pylori infections necessitates a multifaceted approach integrating region-specific therapeutic strategies tailored to local epidemiological profiles and resistance patterns. Firstly, evidence-based clinical guidelines must be refined to ensure adaptability across diverse healthcare settings, complemented by targeted training programs to enhance implementation in resource-limited areas. Moreover, the global challenge of antimicrobial resistance demands urgent action, including the establishment of robust antibiotic stewardship programs and advanced surveillance systems. Achieving these objectives requires sustained investment in translational research, dynamic policy frameworks, and international collaboration to foster data sharing and resource allocation, ultimately advancing global health outcomes.

Conclusion

This study systematically evaluated global variations in Helicobacter pylori management guidelines to address disparities in diagnostic criteria, treatment strategies, and eradication indications across diverse geographical and socioeconomic contexts. Through a rigorous systematic review of 25 guidelines (2014–2024).

Notably, divergent recommendations emerged in critical areas: (1) eradication indications, where gastroesophageal reflux disease (GERD) management split guidelines into opposing camps—some advocating eradication for long-term proton pump inhibitor users, others cautioning against it due to potential protective effects; (2) diagnostic methodologies, with serological testing controversially endorsed in low-resource settings despite limitations in differentiating active infections; and (3) treatment strategies, where bismuth quadruple therapy and concomitant therapy are increasingly favored over clarithromycin-based regimens in regions with rising antibiotic resistance.

The study underscores the urgent need for harmonized, evidence-based guidelines to address regional disparities. For clinicians, our recommendation is that clinical practice should prioritize regionally tailored approaches, integrating local guidelines while maintaining awareness of international recommendations to optimize decision-making. For researchers and health authorities, recommendations include (1) conducting multinational trials to resolve conflicting recommendations; (2) standardizing guideline development using frameworks like GRADE and AGREE II to enhance methodological rigor and stakeholder inclusivity; and (3) establishing dynamic update mechanisms, informed by real-time antimicrobial resistance surveillance, to ensure guidelines remain responsive to evolving epidemiological and therapeutic landscapes. By bridging gaps between global evidence and local implementation challenges, this work provides a foundation for optimizing H. pylori management, advancing gastric cancer prevention, and strengthening antimicrobial stewardship worldwide.

The limitations of this study include: limited geographic coverage, as guidelines and data were retrieved from only 20 countries; lack of regional data within large countries (e.g., differences between sub-regions like China's coastal vs. inland areas); variation in guideline update timing, with some recently revised and others older; and inconsistent methodological standards across guidelines. These limitations highlight the need for further research to address regional variability and standardize methodology.

Supplementary Information

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Supplementary Material 1: Table S1. Detailed treatment information.

Supplementary Material 2: Table S2. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.

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Author's contributions
All the authors contributed to the preparation of this work. M.Y.S. and M.H. drafted and revised the article; H.J.C. was responsible for the theme, final editing, and preparation of the manuscript for submission; L.W.Y. and E.Y.L. critically revised the manuscript. All authors read and approved the final manuscript.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Declarations

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Competing interests
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